Considerable variation has occurred in the definition of the study population among the studies in which the relationship of cigarette smoking to fetal mortality (other than abortion) and early infant mortality was examined. The most commonly identified study populations have been perinatal deaths, neonatal deaths, and late fetal plus neonatal deaths. Perinatal deaths are a combination of late fetal deaths (i.e., stillborn infants) and deaths occurring within the first week of life. Neonatal deaths include all deaths of liveborn infants within the first 28 days of life.

Epidemiological Studies

Most of the earlier epidemiological studies of the association between cigarette smoking and late fetal plus neonatal mortality were reviewed in the 1971 and 1972 reports on the health consequences of smoking (*101*, *102*). A review of previously unreported studies (*67*, *76*), as well as reexamination of previously cited studies, forms the basis of the following statements:

The results of several prospective and retrospective studies indicate a statistically significant higher late fetal and/or neonatal mortality for the infants of smokers compared to those of nonsmokers (*14*, *17*, *25*, *43*). The results of other prospective and retrospective studies identified no significant difference in the mortality rates between the infants of smokers and nonsmokers (*20*, *65*, *72*, *85*, *100*, *115*).

If mortality rates were compared for those infants of smokers and nonsmokers weighing less than 2,500 grams, the infants of nonsmokers apparently had a considerably higher risk than did those of smokers.

The results of recent studies, coupled with a critical review of the design and analysis of previous studies, and a reexamination of existing data, may provide at least a partial explanation of discrepancies between the results of previous studies.

Comparisons of the Mortality Risks of Low-Birth-Weight Infants Born to Smokers and Nonsmokers

The perinatal mortality risk for infants weighing less than 2,500 grams appears to be lower for those infants born to women who smoke during pregnancy than for those born to nonsmokers (table

3). However, available evidence shows that cigarette smokers' infants tend to be small-for-gestational age rather than gestationally premature. Hence, within a given birth weight group, the infants of smokers are, on the average, gestationally more mature than those of nonsmokers. Data collected by the National Center for Health Statistics (*103*) demonstrate that within a given birth weight group, the more gestationally mature an infant, the lower is its mortality risk (fig. 6). Thus, the difference in perinatal mortality risks experienced by the infants of cigarette smokers and nonsmokers, within comparable birth weight classes, reflects the facts that the two sets of infants are not of the same average gestational age, and that gestational age is a major factor influencing late fetal and neonatal mortality. An accurate estimate of comparative mortality risks for the infants of cigarette smokers and nonsmokers requires adjustment for gestational age.

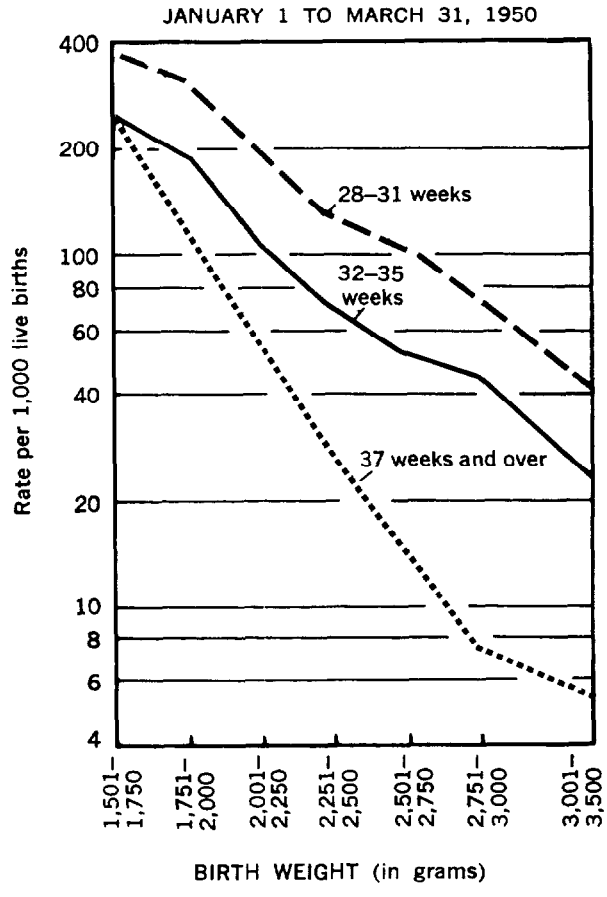
For infants of comparable gestational age, lower birth weight is associated with higher mortality (fig. 6). Since infants of cigarette smokers have, on the average, lower birth weights than the infants of nonsmokers, within groups of comparable gestational age, cigarette smokers' infants should experience higher mortality rates than nonsmokers' infants of similar gestational ages. In a recent review, Meyer and Comstock (*51*) provided a more extensive discussion of these points.

TABLE 3.—*Comparison of the perinatal mortality for infants weighing less than 2,500 grams, of smokers and nonsmokers*

Author, reference	Perinatal mortality rate (deaths per 1,000 live births)	
	Smokers	Nonsmokers
Underwood, et al. (*100*)	187	269
Ontario Department of Health (*67*)	232	300
Kullander and Källen (*43*)	129	139
Rantakallio (*76*)	288	344
Yerushalmy [1] (*112*):		
Black women	114	202
White women	114	218
Butler and Alberman (*14*)	269	284

[1] Reported neonatal mortality rates only.

Figure 6.—Neonatal mortality rates among single white births in hospitals (by detailed birth weight and specified gestation groups: United States).

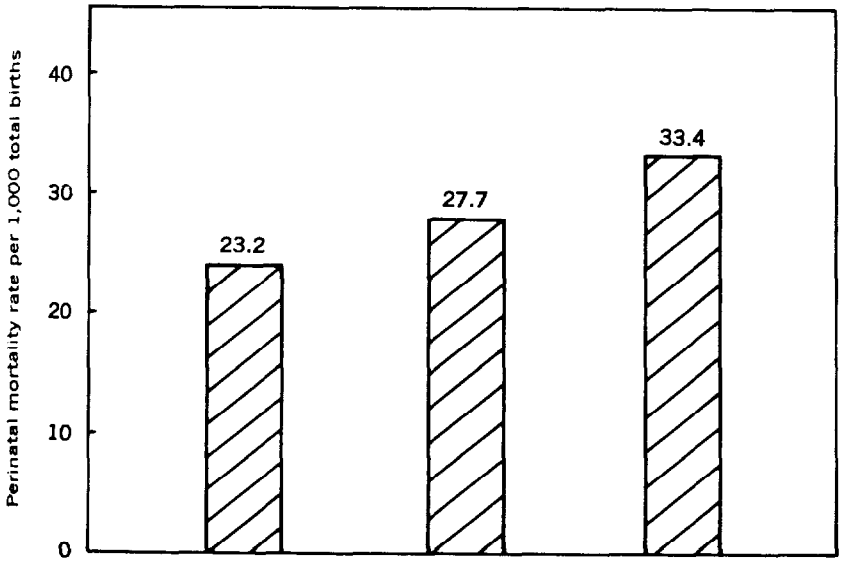


SOURCE: U.S. Public Health Service, National Center for Health Statistics (103).

Recent Studies

The Ontario Perinatal Mortality Study (*66*, *67*) was conducted among 10 teaching hospitals during 1960 and 1961. In this retrospective study of 51,490 pregnancies, a statistically significant increase in the perinatal mortality rate was demonstrated for smokers' infants as compared with those of nonsmokers; the infants of smokers experienced an overall relative risk of 1.27 ($P<0.001$). Moreover, the investigators found a statistically significant dose-response relationship between the amount of cigarettes smoked and the perinatal mortality rate ($P<0.001$) (fig. 7).

Figure 7.—Perinatal mortality rate per 1,000 total births by cigarette smoking category.



	Nonsmoker	<1 pack of cigarettes per day	≧1 pack of cigarettes per day
Number of perinatal deaths:	659	425	220
Total births:	28,358	15,328	6,581

(P <0.001)

SOURCE: Ontario Department of Health *(66)*.

Recently Butler, et al. (*15*) further analyzed the British Perinatal Mortality Study. They found a highly significant association between maternal smoking after the fourth month of pregnancy and both late fetal and neonatal deaths. Infants of smokers had an increase in the late fetal mortality rate of 30 percent, and an increase in the neonatal mortality rate of 26 percent, compared to the infants of nonsmokers. The overall mortality ratio of late fetal plus neonatal deaths was 1.28 ($P<0.001$). Given the large number of women in the study, and the significant changes in smoking behavior which occurred, they found it possible to consider the effect of a change in smoking

behavior between the beginning of pregnancy and the fourth month on late fetal and neonatal mortality. A statistically significant and dose-related increase in mortality occurred among the infants of mothers who continued to smoke after the fourth month of pregnancy, as compared with the infants of nonsmokers and those of women who smoked prior to the pregnancy but gave up smoking by the fourth month of gestation.

Niswander and Gordon (*63*) reported data from the prospective Collaborative Perinatal Study of the National Institute of Neurological Disease and Stroke. The 39,215 pregnancies registered at 12 university hospitals in the United States were almost equally divided between black and white women. They found a nonsignificant increase in perinatal mortality among the infants of white smokers as compared to those of white nonsmokers; the overall mortality ratio was 1.13 ($P>0.1$). The infants of black smokers, however, had a significantly higher mortality risk than did those of black nonsmokers; the mortality ratio was 1.18 ($P<0.02$). Moreover, a definite dose-response relationship between cigarettes smoked by pregnant mothers and mortality risk was shown for black infants. Black women were noted to smoke significantly fewer cigarettes, on the average, than white women.

Rush and Kass (*82*) found, in a prospective study of 3,276 pregnancies followed at Boston City Hospital, a nonsignificant increase in late fetal plus neonatal mortality rate among the infants of white women who smoked as compared to those of white nonsmokers. However, the infants of black women who smoked had a statistically significant increase in mortality rate compared to the infants of black nonsmokers ($P<0.01$). The overall mortality ratio for black women who smoked was 1.86. The difference in frequency of stillbirth among the infants of smokers and nonsmokers was the primary factor which contributed to the significance of the difference in mortality rates.

Analysis of Previously Reported Studies

Previously reported studies can be divided into two groups: A group in which the late fetal plus neonatal mortality rates for infants born to cigarette smokers were significantly higher than those for the infants born to nonsmokers, and a group in which no significant differences were detected in the mortality rates for the infants born to smokers and nonsmokers. The results of several studies (*14*, *17*, *25*, *42*, *43*, *55*, *84*, *92*) yielded mortality ratios ranging from 1.38 to 1.78. The results of other studies (*20*, *65*, *76*, *85*, *100*, *115*) yielded mortality ratios ranging from 1.01 to 1.06. Both groups contained retrospective and prospective studies of comparable size. The two groups did differ

significantly, however, with regard to control of variables other than cigarette smoking which influence perinatal mortality.

Factors Which Influence Perinatal Mortality Other Than Smoking

Butler and Alberman (*13*), on data from the British Perinatal Mortality Study, employed a logit transformation analysis of variance, and demonstrated that maternal height, age, parity, social class, and severe preeclampsia all had a significant independent effect on late fetal and neonatal mortality. Rumeau-Roquette (*81*) provided evidence that a previous stillbirth or low-birth-weight infant significantly increased the risk of a future stillbirth. Meyer and Comstock (*51*) provided examples of how the differential distribution of smoking and other factors which are related to perinatal mortality, in a population of women, can bias data (e.g., black women have higher perinatal mortality rates than do white women, but black women smoke less than white women do. Hence, nonsmokers will tend to include more black women, and smokers more white women. This will tend to reduce any differences between the groups in mortality rates.) Meyer and Comstock concluded, "Comparisons of mortality rates of smokers' and nonsmokers' babies should be made within subgroups according to parity, socioeconomic status, and other appropriate risk factors, and not separated by birth weight."

In three of the studies in which a significantly higher mortality risk was demonstrated for the infants of smokers, adjustment for other variables was performed. The results indicated that, after such adjustment, a significant independent association between cigarette smoking and infant mortality persisted (*13* and *15*, *17*, *81*). Of the studies which revealed no significant increase in mortality risks for smokers' infants, one (*115*) controlled for race alone. Hence, at least part of the discrepancy in results between the two groups of studies may be explained by a lack of control of variables other than smoking.

Another possible, at least partial, explanation of the discrepancy in results obtained by the two sets of studies is that cigarette smoke may be more harmful to the fetuses of certain women than others. Several developing lines of evidence suggest that this may be the case:

1. Cigarette smoking and socioeconomic background.

Butler, et al. (*15*) noted that when data from the British Perinatal Mortality Study are grouped by social class of the mother's husband, the late fetal plus neonatal mortality ratio for infants of smokers and nonsmokers in the upper social classes I and II is 1.10; the mortality ratio for the entire sample was 1.28. Rush and Kass (*82*) reviewed the British Perinatal Mortality Study, along with several other studies, and noted that all have shown the strongest association between excess infant mortality and cigarette smoking among the infants of those

mothers with lower socioeconomic status. Comstock and Lundin (*16*) found excess mortality among smokers' infants almost entirely confined to those whose fathers had a grammar school education or less. Several of the studies which revealed no significant difference in mortality among the infants of smokers and nonsmokers were conducted in predominately middle class populations (*20*, *100*, *115*).

2. Cigarette smoking and previous obstetrical experience.

Peterson, et al. (*72*) had rigid criteria for entry into his study population of 7,740 women. He included only those women who previously had healthy infants with a birth weight greater than 2,500 grams. He found a significant decrease in birth weight among smokers' infants, but no significant increase in mortality rates. Rumeau-Roquette (*81*) found that among women who previously had delivered only healthy infants weighing more than 2,500 grams, cigarette smoking was not associated with an increased risk of stillbirth; among those women with a previous stillbirth, smoking was significantly associated with increased risk of a future stillbirth.

3. Cigarette smoking and genetic differences.

The consistent finding that the mortality risk for the infants of black smokers is higher than the risk for the infants of white smokers, even when the socioeconomic background for both is ostensibly similar, suggests that genetic factors also may interact with smoking to produce enhanced risk (*82*, *99*, *115*).

Available evidence suggests that if those women, who are already likely to have small infants for reasons other than smoking, smoke during pregnancy, their infants will be most unfavorably affected. This means that the women in the United States whose infants will be most affected by cigarette smoking are those who have an unfavorable socioeconomic situation, have a history of previously unsuccessful pregnancies, and are black.

Experimental Studies

Studies in Animals

Studies previously reviewed in the 1971 and 1972 reports on the health consequences of smoking (*101*, *102*) demonstrate that exposure of rabbits and rats to tobacco smoke and to injections of large doses of nicotine resulted in significantly increased late fetal and neonatal mortality. Astrup (*2*) has recently studied the effect of continuous exposure of pregnant rabbits to carbon monoxide on stillbirth rates. He found a significantly higher, dose-related incidence of stillbirths and deaths within the first 24 hours of life among the offspring of the experimental rabbits (table 4).

TABLE 4.—*Effect of carbon monoxide exposure of pregnant rabbits on birth weight and neonatal mortality*

	Group 1, 0 percent COHb	Group 2, 8 to 10 percent COHb	Group 3, 16 to 18 percent COHb
Number of pregnant rabbits	17	14	17
Total number of babies	116	81	123
Stillborn and babies died within first 24 hours	[1] 1	[2] 8	[3] 44
		($P<0.001$)	

[1] 1 percent.
[2] 10 percent.
[3] 36 percent.
Source: Astrup, P. (*2*).

Studies in Humans

Some investigators have examined the causes of death among the infants of smokers as compared with those of nonsmokers. Comstock, et al. (*17*) found that infants of smokers died more frequently of asphyxia, atelectasis, and immaturity. Kullander and Källen (*43*) found abruptio placentae significantly increased as a cause of death among smokers' infants. Butler and Alberman (*14*) found little difference in the death rates for the infants of smokers and nonsmokers from isoimmunization and malformations, but higher rates were found for smokers' infants in the groups in which death occurred before or during labor, or in which death resulted from massive pulmonary hemorrhage, or pulmonary infection. As the authors noted, "The latter three are conditions known to be associated with small-for-dates babies." They pointed out that distribution of causes of death in the smoking group could be accounted for almost entirely by the excess of low-birthweight babies. This supports the conclusion that the mechanism which affects birth weight also influences mortality.

SIGNIFICANCE OF THE ASSOCIATION

The following calculation is offered to give some idea of the order of magnitude of increased late fetal and neonatal mortality associated with cigarette smoking during pregnancy. If women who smoked dur-

ing pregnancy in the United States had an elevation in risk of 28 percent for late fetal and neonatal mortality, as demonstrated by Butler, et al. (*15*) for Britain, Scotland, and Wales, and if 20 percent of pregnant women smoked throughout the pregnancy,[1] the higher risk of stillbirth and neonatal death for the infants of mothers who smoke cigarettes during pregnancy would account for approximately 4,600 of the 87,263 stillbirth and neonatal deaths in the United States in 1968.

Late Fetal and Neonatal Death Summary

A strong, probably causal association between cigarette smoking and higher late fetal and infant mortality among smokers' infants is supported by the following evidence:

1. Twelve retrospective and prospective studies have revealed a statistically significant relationship between cigarette smoking and an elevated mortality risk among the infants of smokers. In three of these studies, of sufficient size to permit adjustment for other risk factors, a highly significant independent association between smokng and mortality was established. Part of the discrepancy in results between these studies and those in which a significant association between smoking and infant mortality was not demonstrated may be explained by a lack of adjustment for risk factors other than smoking.
2. Evidence is converging to suggest that cigarette smoking may be more harmful to the infants of some women than others; this may also, in part, explain the discrepancies between the results of the studies in which a significantly higher mortality risk was shown for the infants of smokers compared to those of nonsmokers and the results of those studies in which significant differences in mortality risk were not found.
3. Within groups of similar birth weight, the infants of nonsmokers appear to have a higher mortality risk than do the infants of cigarette smokers. This results from the fact that the infants of nonsmokers within such similar birth weight groups are on the average gestationally less mature than the infants of cigarette smokers. Available evidence indicates that within groups of similar gestational age, infants of lower birth weight experience a higher mortality risk. Since the infants of cigarette smokers are

[1] Based on extrapolation of data on smoking behavior change during pregnancy from the British Perinatal Mortality Study, which probably yields a conservative estimate.

small-for-gestational age, one should expect that if the infants of cigarette smokers and nonsmokers are compared within similar gestational age classes, the infants of cigarette smokers would have the higher mortality rate.

4. The results of recent studies have documented a statistically significant dose-response relationship between the number or amount of cigarettes smoked and late fetal and neonatal mortality.
5. New data suggest that if a woman gives up smoking by the fourth month of pregnancy, she will have the same risk of incurring a fetal or neonatal loss as a nonsmoker.
6. Available evidence strongly supports cigarette smoking as one cause of fetal growth retardation. The causes of excess deaths among the infants of smokers are those associated with small-for-dates babies.
7. Data from experiments in animals have demonstrated that exposure to tobacco smoke or some of its ingredients, such as nicotine or carbon monoxide, results in a significant increase in late fetal and or neonatal deaths.
8. The results of studies in humans have shown that the fetus of a smoking mother may be directly exposed to agents such as carbon monoxide within tobacco smoke, at levels comparable to those which have been shown to produce stillbirth in experimental animals.

Sex Ratio

Although a number of small studies have found a slight, usually statistically nonsignificant, increase in the proportion of female infants born to smokers, the three largest studies of Underwood, et al. (48,505 pregnancies), Butler (15,791 pregnancies), and MacMahon (12,155 pregnancies) have found similar infant sex ratios among both smoking and nonsmoking mothers, with the expected slight excess of males among each (table 5).

Summary

Available evidence strongly indicates that maternal cigarette smoking does not influence the sex ratio of newborn infants.

TABLE 5.—*Proportion of male infants delivered to smoking and nonsmoking mothers*

Author, reference	Pregnancies	Proportion of male infants		Statistical significance
		Smokers	Nonsmokers	
Underwood, et al. (*100*)	48, 505	.518	.519	None.
Butler and Alberman (*14*)	15, 791	.518	.516	Do.
MacMahon, et al. (*49*)	12, 155	.513	.512	Do.
Kullander and Källen (*43*)	6, 363	.515	.501	Do.
Reinke and Henderson [1](*78*)	3, 156	.498	.517	Do.
Frazier, et al.[1] (*25*)	2, 915	.472	.505	Do.
				(P>0.05)
Kizer (*42*)	2, 095	.502	.493	None.
Herriott, et al. (*35*)	2, 745	.492	.517	Do.
Ravenholt, et al (*77*)	2, 052	.501	.533	P<0.05
Lowe (*46*)	2, 042	.532	.529	None.
Russell, et al. (*83*)	2, 002	.513	.512	Do.

[1] Black women.

Congenital Malformations

Previous epidemiological studies which examined the relationship between cigarette smoking and congenital malformations were reviewed in the 1971 and 1972 reports on the health consequences of smoking (*101*, *102*). Recently, the authors of the Ontario Perinatal Mortality Study (*66*, *67*), a retrospective study of 51,490 births, reported no difference in malformation rate for the infants of smokers and nonsmokers. The various studies of the association between cigarette smoking and congenital malformation have differed significantly with regard to study design, the type of population sampled, sample size and number of infants with malformations, the definition of malformation, and results (table 6).

Previous experimental work was reviewed in the 1971 and 1972 reports on the health consequences of smoking (*101*, *102*). The chick embryo has been employed in recent studies. The direct application of nicotine to the embryo results in cephalic hematomas (*26*), malformations of the cervical vertebrae (*93*), and anomalies of the heart (*27*), depending upon dose of nicotine and period of incubation in which exposure occurs. Anomalies of the limbs of chicken embryos can also be induced by exposure of the egg to high levels of carbon monoxide (*4*).

TABLE 6.—*Relative risk of congenital malformation for infants of cigarette smokers and nonsmokers, comparing available studies with regard to study design, study population, sample size, number of infants with malformations, and definition of malformation*

Author, reference	Study design	Study population	Sample size	Infants with malformations	Relative risk SM/NS	Definition of malformations
Lowe (*46*)	Retrospective	Stillborn plus 24-hour deaths.	2,042	23	1.36	Major.
Comstock, et al. (*17*).	do	Neonatal deaths	236	37	.31	Major, cause of death.
Yerushalmy (*112*)	Prospective	Infants less than 2,500 g.	695	59	.57	Major.
Ontario Department of Health (*67*).	Retrospective	Stillborn plus 1st-week deaths plus surviving infants.	51,490	1,744	.97	
Butler and Alberman (*14*).	do	Stillborn plus neonatal deaths.	7,123	1,382	1.19	Major, cause of death.
Kullander and Källen (*43*).	Prospective	(a) Stillborn plus neonatal deaths plus remainder of deaths to age 1.	137	43	1.25	Major and minor malformations.
		(b) Surviving infants to age 1.	4,903	700	1.06	
Fedrick, et al. (*24*).	Retrospective	(a) [1] Stillborn plus neonatal deaths [1] and deaths to age 7,[1] survivors [2] to age 7.	17,418	86	1.55	(1).
		(b) Neonatal deaths [1] (3-month study).	7,822	204	1.07	(2).

[1] Autopsy-proven congenital cardiac malformation.
[2] Clinically determined congenital heart disease.

Congenital Malformation Summary

Given the considerable variation in study design, study population, sample size, number of affected infants, definition of malformation, and results, no conclusions can be drawn about any relationship between maternal cigarette smoking and congenital malformation at the present time.

Lactation

Introduction

The following section is a review of available evidence which bears upon any interaction between cigarette smoking and lactation. Emphasis is placed upon the relationship of cigarette smoking to the quantity of milk produced, to the presence of constituents of cigarette smoke within the milk, and to effects upon the nursing infant mediated through changes in either the quantity of milk available or the substances within the milk.

Epidemiological Studies

Underwood, et al. (*99*), in a study of 2,000 women from various social and economic strata, observed a definite but statistically insignificant trend toward more frequent inadequacy of breast milk production among those smoking mothers who attempted to nurse compared to nonsmokers.

Mills (*52*), in a study of 520 women, found that among women who indicated either a desire to nurse or no desire to nurse yet continued to nurse beyond 10 days, and who had delivered their first live-born infant, the average period of nursing for mothers who smoked was significantly shorter than for nonsmokers. Moreover, among the 24 mothers who had given up smoking during at least the final 3 months of their pregnancies, the average length of nursing was identical to that of the nonsmokers. There was no significant difference between smokers and nonsmokers with regard to complete inability to nurse their offspring. This study is difficult to interpret because the author did not determine the reason(s) for the discontinuation of nursing among the women.

Experimental Studies

Studies in Animals

Nicotine

Influence on the Lactation Process

Blake and Sawyer (*11*) studied the influence of subcutaneously injected nicotine (4 mg. total over a 5-minute period) upon lactation in the rat. They found that nicotine inhibited the suckling-induced

rise in prolactin. No effect of injected nicotine was demonstrated for oxytocin secretion since milk release was not blocked.

Wilson (*110*) examined the effects of nicotine supplied through drinking water (0.5, 1.0, and 2.0 mg. daily) on the weight gain of nursing rats. Apparently, the nicotine had been available throughout gestation as well, because the author commented on a reduction in litter size among the experimental groups, more or less proportionate to the dose of nicotine; hence, a prenatal effect could not have been distinguished from a postnatal one. Average birth weight was similar for experimental and control groups. No difference in weight gain was seen for any of the groups. The lack of impact on birth weight suggests that dose was lower than that used in other studies.

Presence of Nicotine in the Milk

Hatcher and Crosby (*32*), using a frog bioassay, reported traces of nicotine in cow's milk 24 hours after the intramuscular injection of 5.0 mg./kg. and 5 hours after the injection of 0.5 mg./kg.

Evidence for an Effect Upon the Nursing Offspring

Hatcher and Crosby (*32*) found that 0.5 mg./kg. nicotine injected into nursing cats had no apparent harmful effect upon the kittens. Apparently 4.0 mg./kg. suppressed lactation. Kittens fed the milk from the cow which had been injected with 5.0 mg./kg. nicotine were also apparently unaffected.

Nitrosamines

Mohr (*53*) found that diethylnitrosamine and dibutylnitrosamine, when administered to lactating hamsters, were associated with the development of typical tracheal papillary tumors in the young, suggesting passage of these compounds in the milk. Although diethylnitrosamine and dibutylnitrosamine have not been identified in cigarette smoke, many N-nitrosamines are potent carcinogens, and some of them are present in cigarette smoke (*37*, *79*).

Studies in Humans

Nicotine and/or Tobacco Smoke

Influence on the Lactation Process

Emanuel (*22*) noted no reduction in milk production among 10 wet nurses who were encouraged to smoke seven to 15 cigarettes daily;

some were observed to inhale the smoke. Hatcher and Crosby (*32*) noted that after a mother smoked seven cigarettes within 2 hours, it was difficult to obtain a specimen of breast milk. Perlman, et al. (*71*) found that of 55 women smokers with an adequate milk supply at the beginning of his study, 11 (20 percent) of the women had an inadequate supply at the time of discharge from the hospital. No relationship was reported between the number of cigarettes smoked and the likelihood of developing an inadequate milk supply. The authors' impression was that there was no greater proportion with an inadequate milk supply among smokers than among nonsmokers, but no corroborating data were supplied.

Presence of Nicotine in the Milk

Hatcher and Crosby (*32*) found, using a frog bioassay, that the milk of a woman collected after she had smoked seven cigarettes in 2 hours contained approximately 0.6 mg./liter nicotine. Emanuel (*22*), using a leech bioassay, studied excretion of nicotine in the milk of wet nurses who were encouraged to smoke for the experiment. After the subjects had smoked six to 15 cigarettes over a 1- to 2-hour period, the author found nicotine in their milk 4 to 5 hours after smoking, with a maximum concentration of 0.03 mg./liter. Bisdom (*10*) demonstrated nicotine in the milk of a mother who smoked 20 cigarettes a day. Thompson (*97*) found approximately 0.1 mg./liter of nicotine in the milk of a mother who smoked nine cigarettes a day (plus three pipefuls). Perlman, et al. (*71*), using a Daphnia bioassay, demonstrated nicotine in the milk of all women who smoked in their study. Moreover, they found a direct dose-relationship between concentration of nicotine and the number of cigarettes smoked. No comment is made by the authors on the possible inaccuracy introduced by examining only the residual milk following nursing, but it is well known that the composition of the fore milk and hind milk is different and perhaps the concentration of nicotine also differs.

Evidence for a Clinical Effect Upon the Offspring

Emanuel (*22*) noted that among the infants in his study, loose stools were observed only in the one whose wet nurse had smoked 20 cigarettes in the previous 4 hours. Bisdom (*10*) observed a case of "nicotine poisoning" in a 6-week-old infant whose mother smoked 20 cigarettes a day. The symptoms included: restlessness, vomiting, diarrhea, and tachycardia. Nicotine was demonstrated in the milk, and the symptoms abated when smoking was stopped. Greiner (*30*) also described a case of possible nicotine poisoning in a 3-week-old nursling

whose mother smoked 35 to 40 cigarettes a day. The symptoms included vomiting and loose stools. Following the curtailment of smoking, the symptoms gradually abated over a 3-day period. Perlman, et al. (*71*) noted no effect of smoking on the weight gain of the infants of the smokers in their study. Furthermore, no untoward symptoms were observed. They therefore doubted an effect of smoking on lactation. They noted that the dose received by the infants was beneath the toxic level as computed from adult experience, and this accorded with their clinical observations. The fact that they admitted to the study only women with an apparently adequate milk supply may have affected their results. The authors suggested that perhaps the lack of effect of smoking upon lactation might represent the development of tolerance to nicotine, as both the mother and the offspring had been exposed throughout the pregnancy.

VITAMIN C

Venulet (*105*, *106*, *107*), in a series of studies, demonstrated that the level of vitamin C was reduced in the milk of smoking mothers as compared with nonsmokers. The clinical significance of this observation has not been evaluated.

Lactation Summary

1. The two pertinent epidemiological studies suggest a possible influence of smoking upon the adequacy of milk supply However, with only limited numbers of women and without control of other potentially significant variables, no conclusions can be drawn.
2. Studies in rats have demonstrated that nicotine can interfere with suckling-induced rise in prolactin. The relevance for humans is uncertain.
3. Evidence exists that nicotine passes into breast milk. No clear evidence for an acute effect upon the nursing infant is available. Potential chronic effects have not been studied.
4. New evidence from experiments with mice suggests that nitrosamines, known carcinogens, pass through the milk to suckling young.

Preeclampsia

Previous epidemiological studies of the relationship between cigarette smoking and preeclampsia were reviewed in the 1971 and 1972 reports on the health consequences of smoking (*101*, *102*) and form the basis of the following statements:

The results of several large prospective and retrospective studies indicate a statistically significant lower incidence of preeclampsia among smoking women (*14*, *43*, *100*). The results of one large retrospective study demonstrated a significant inverse relationship between the incidence of preeclampsia and the number of cigarettes smoked (*100*). When other risk factors, such as parity, social class, maternal weight before the pregnancy, and maternal weight gain during the pregnancy were controlled, smoking women retained a significantly decreased risk of preeclampsia (*21*). The lower risk of preeclampsia for cigarette smoking women has been demonstrated in Britain and Scotland (*14*, *21*, *46*, *83*), The United States (*100*, *118*), Venezuela (*42*), and Sweden (*43*). If a maternal smoker does develop preeclampsia, however, available data suggest that her infant has a higher mortality risk than does the infant of a nonsmoker with preeclampsia (*21*, *83*).

Summary

1. Available evidence indicates that maternal cigarette smokers have a significantly lower risk of developing preeclampsia as compared to nonsmokers.
2. If a woman who smokes cigarettes during pregnancy does develop preeclampsia, her infant has a higher mortality risk than the infant of a nonsmoker with preeclampsia.

Pregnancy References

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